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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,806	05/22/2001	David Sidransky	JHUI160-3	9575

7590 07/14/2003
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EXAMINER

ZITOMER, STEPHANIE W

ART UNIT PAPER NUMBER

1634

DATE MAILED: 07/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary**Application No.**

09/863,806

Applicant(s)

SIDRANSKY, DAVID

Examiner

Stephanie Zitomer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 May 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

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DETAILED ACTION

Application status

1. Receipt of applicant's Response to the Restriction Requirement filed March 3, 2003 with election with traverse of SEQ ID NOS:3 and 4 for the target nucleotide sequences and SEQ ID NOS:35 and 36 for the primers is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Rejections not reiterated herein from the prior Office action mailed September 24, 2002 have been withdrawn. Notably, the amendments to claim 1 have obviated the double patenting obviousness-type rejection. A new double patenting obviousness-type rejection has been made herein.

Objection oath and first sentence of specification: Incorrect patent number

3. The patent number, 5,726,223, given for application serial number 08/579,233, is incorrect. The correct patent number is 5,726,019.

The incorrect patent number also appears in the first sentence of the specification.

Appropriate corrections are required.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejection under 35 U.S.C. 112, first paragraph: Lack of written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the

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specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1-7 are drawn to a method for detecting cancer in a subject via amplification of a target mutant nucleotide sequence in a saliva specimen with primers having SEQ ID NOS:35 and 36 followed by detecting the target nucleotide sequence in the amplification product. Claims 8-11 are drawn to a method for detecting cancer in a subject via contacting nucleic acid from a saliva specimen with an oligonucleotide probe that hybridizes to a target mutant nucleotide sequence having SEQ ID NO:3 or 4 and detecting hybridization of the probe. There are two aspects of the claims that lack support in the disclosure: (a) the broad scope of "cancer" and (b) the relationship between "cancer" and the elected nucleotide sequences, SEQ ID NOS:3, 4, 35 and 36.

(a) The term, "cancer", constitutes a large genus of cancer types such as sarcoma, carcinoma, melanoma, lymphoma, myeloma, etc., named for the tissue in which they arise. However, the specification discloses only carcinomas, which are cancers of epithelial origin, particularly of the head, neck and lungs (pages 5, 6, 11 and 41, original specification), cancers which one of ordinary skill in the art would have expected to be detectable in saliva. Furthermore, analysis of nucleotide sequences in saliva is described in the specification as based on obtaining sample DNA from **epithelial** cells (page 12,, page 35, line 17, and page 41, original specification). Therefore, the disclosure lacks written description of a representative number of species of cancer types to support the broad term, "cancer" in the claimed methods.

(b) The "target mutant nucleotide sequence" of the claimed invention is presumed to be a microsatellite marker sequence designated D21S1245 because the primer sequences set forth at page 22 (original specification) are so designated and the format of the number is one commonly used in the art for microsatellite marker sequences. With regard to the relationship of this marker sequence and "cancer", the specification fails to provide any information linking the two. Furthermore, in the general discussion of "mutation", the specification points out the well-

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established facts that mutations do not always lead to cancer, that is, they may be silent (page 10, original specification); that a major type of DNA polymorphism is found in microsatellites (page 10, original specification); and "mutant nucleotide sequences [are] associated with benign as well as malignant neoplasias (cancer)" (page 11, original specification). There is absolutely no information establishing correspondence of SEQ ID NOS: 3, 4, 35 and 36 with "cancer". Therefore, the specification fails to provide any written descriptive support for the claimed methods of detecting cancer in a subject by detecting D21S1245 microsatellite sequences in the subject's saliva. In addition to enablement the first paragraph of 112 requires a "written description". As set forth by the Court in *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. Absent a description of the requisite representative number of "cancer" species and information relating SEQ ID NOS: 3, 4, 35 and 36 to "cancer", the written description clearly fails to convey to one of skill in the art that applicant was in possession of the claimed invention method at the time the claimed invention was filed.

Rejections under 35 U.S.C. 112, second paragraph: Indefiniteness

5. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) The claims are confusing in reciting nonelected subject matter. Appropriate correction is required.

(b) Claims 1-7 lack antecedent basis for the recitation in the last two lines, "wherein the presence of the target mutant nucleotide sequence is indicative of cancer in the subject" because the preceding method steps do not relate "target mutant nucleotide sequence" to "cancer".

(c) Claims 5-11 are indefinite because the terms "selective" and "selectively" are relative terms. The terms are not defined by the claim, the specification does not provide a

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standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested to delete the offending terms.

Prior art of interest

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The patent to Stroun et al., 5,952,170, discloses a method for diagnosing cancer by analyzing DNA in blood plasma. SEQ ID NO:18 in the Sequence Listing is the same as applicant's SEQ ID NO:36 but the function of SEQ ID NO:18 is not described in the specification or in the claims.

Conclusion

7. **No claim is allowed.**

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

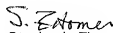
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 9:00 am to 11 am and 1:00 pm to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724. The examiner's Rightfax number is 703-746-3148.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196. For questions and requests relating to formal matters contact LIE Chantae Dessau at 703-605-1237.


Stephanie Zitomer, Ph.D.
July 2, 2003

STEPHANIE W. ZITOMER
PRIMARY EXAMINER